## **Amendments to the Specification:**

On page 3, amend the paragraph beginning on line 1 as follows:

In one aspect, the invention includes a liposome composition containing a lipid represented by the formula:

wherein each of  $R^1$  and  $R^2$  is an alkyl or alkenyl chain having between about 8 to about 24 carbon atoms;  $n = \underline{10}$ -20; L is selected from the group consisting of (I) -X-(C=O)-Y- $CH_2$ -, (ii) -X-(C=O)-, and (iii) -X- $CH_2$ -, wherein X and Y are independently selected from oxygen, NH, and a direct bond; and Z is a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0.

On page 6, amend the paragraph beginning on line 19 as follows:

In one aspect, the invention includes lipids represented by the structure shown below:

wherein each of  $R^1$  and  $R^2$  is an alkyl or alkenyl chain having between about 8 to about 24 carbon atoms;  $n = \underline{40}$ -20; and in a preferred embodiment is between 1-10; L is selected from the group consisting of (i) -X-(C=O)-Y- $-CH_2$ -, (ii) -X-(C=O)-, and (iii) -X-CH<sub>2</sub>-, wherein X and Y are independently selected from oxygen, NH, and a direct bond; and Z is a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0.

## On page 7, amend the paragraph beginning on line 15 as follows:

The lipids of the invention include a neutral linkage, L, joining the Z moiety and the tail portion of the lipid. Linkage L can vary, but in one embodiment is selected from

areld

a carbamate, and ester, and amide, a carbonate, a urea, an amine, and an ether. In a preferred prepared lipid, a carbamate linkage is emplyoed, wherein L is –X-(C=O)-Y-CH<sub>2</sub>-, X is NH, and Y is oxygen.

On page 7, amend the paragraph beginning on line 24 as follows:

The lipid of the invention can be prepared using standard synthetic methods. A lipid was prepared having the structure shown above, wherein Z is an imidazole,  $N_n=2$ , L is a carbamate, and  $R^1=R^2=C_{17}H_{35}$ . A reaction scheme for preparation of this lipid is shown in Fig. 1. Full details of the synthesis are also provided in Example 1. Briefly, the para-nitrophenyl carbonate of 1,2-distearoyl glycerol (Compound I) and paranitrophenyl chloroformate (Compound II) and reacted with histamine (Compound IV), to yield a lipid (compound VI) having an imidazole moiety linked to a distearoyl tail via a carbamate linkage. A similar synthesis, using glycerol in place of 1-amino-2,3-propanediol, can also be used to produce a carbonat-linked product (L = -O-(C=O)-O-CH<sub>2</sub>- or -O-(C=O)-CH<sub>2</sub>-).

On page 8, amend the paragraphs beginning on line 4 and ending on 18 as follows:

Given the guidance and examples herein, other synthesis of a lipid having other linkages can be readily accomplished by those of skill in the art. Other linkage include, for example, ether ( $L = O-CH_2-$ ) and ester linkages (L = -O-(C=O)-), as well as <u>urea</u> amide, <u>urea-and</u> amine linkages (i.e., where L = -NH-(C=O)-NH-,  $-NH-(C=O)-CH_2-$ ,  $-NH-(C=O)-NH-CH_2-$ , or  $-NH-CH_2-$ ). A keto linkage, where LX is a direct bond, may also be prepared. Figs. 2A-2B illustrate preparation of an <u>etheramine-linked lipid</u> (Fig. 2A) and an <u>ester-linked-lipid having an NH-containing linkage</u> (Fig. 2B), respectively. In Fig. 2A, the terminal amine of histamine is reacted with glycidyl chloride, hydrolyzing the resulting epoxide and acylation the resulting diol.

In Fig. 2B, an-ester-linked-lipid having an NH- containing linkage (L = -O-(C=O)-or -O-(C=O)-CH<sub>2</sub>-) is prepared, for example, by reacting histamine with an activated derivative of glyceric acid acetonide (2,2-dimethyl-1,3-dioxolane-4-carboxylic acid) or the four-carbon homolog, 2,2-dimethyl-1,3-dioxolane-4-acetic acid. The diol is subsequently deprotected and acylated.

25